

wherein said composition comprises at least 2 gr of component (i) per 100 gr and 1 gr of component (ii) per 100 grams.

REMARKS

Claims 11-18 and 20-31 are pending. As suggested by the Examiner, claim 11 has been amended to recite particular amounts of acetyl-L-carnitine component (i) and hydroxycitric acid component (ii). Support for the amendment is found *inter alia* at pages 16-20 of the specification. Accordingly, the Applicants do not believe that any new matter has been added.

The Applicants thank Examiner Kishore for the courteous interview of May 28, 2002. As suggested, the claims have now been limited to particular amounts of acetyl-L-carnitine or hydroxycitric acid. Moreover, the Applicants have further elaborated on the demonstrated statistically significant synergy exerted by the claimed combination of acetyl-L-carnitine and hydroxycitric acid. Accordingly, favorable consideration is now respectfully requested.

Rejection--35 U.S.C. 103

Claims 11-18 and 20-31 were rejected under 35 U.S.C. 103(a) as being unpatentable over Wiegand, U.S. Patent 3,810,994 by itself, or in combination with Moffett, U.S. Patent 5,536,516.

The present invention is not obvious over the cited prior art as Wiegand or Moffett do not suggest or provide a reasonable expectation of success that the combination of acetyl-L-carnitine and hydroxycitric acid would exert the synergistic effects shown in Tables 1-5 on pages 16-20 of the specification and in the Declaration submitted January 2, 2002.

For the convenience of the Examiner, the synergistic effects provided by the invention in decreasing body weight increase, lowering triglyceride levels and lowering cholesterol levels are summarized below. As shown in the embolded results in each Table

below, the effects of the combination of acetyl-L-carnitine and HCA are far greater than the effects of either compound alone. The reduction provided by each treatment compared to the control (no treatment) is shown in the right column. As seen in the two right hand columns, the reductions provided by the combination of acetyl-L-carnitine and HCA are significantly greater the combined reductions provided by acetyl-L-carnitine alone or HCA alone.

<u>Table 2: Body Weight Increase</u>	<u>Level</u>	<u>Reduction</u>	<u>%</u>
Control (no acetyl-L-carnitine or HCA)	62.8	-----	
Acetyl-L-carnitine only:	60.4	-2.4	3.8
HCA only:	46.6	-16.2	25.8
Combination of acetyl-L-carnitine and HCA:	31.6	-31.2	49.9

<u>Table 4: Triglyceride level</u>			
Control (no acetyl-L-carnitine or HCA)	195.8	-----	
Acetyl-L-carnitine only:	191.2	-2.4	1.2
HCA only:	170.6	-25.2	12.9
Combination of acetyl-L-carnitine and HCA:	120.4	-75.4	38.5

<u>Table 5: Cholesterol level</u>			
Control (no acetyl-L-carnitine or HCA)	270.5	-----	
Acetyl-L-carnitine only:	266.7	-3.8	1.4
HCA only:	196.6	-73.9	27.3
Combination of acetyl-L-carnitine and HCA:	150.5	-120.0	44.4

Moreover, the Applicants have established the statistical significance of these results using the Students T-test as shown in the prior Declaration. The T-test is a conventional statistical method for determining the significance of differences between different samples of experimental data, see Statistics, CliffsQuickReview, Hungry Minds, Inc., New York (2001, attached). These T-test results form part of the factual evidence provided in the prior Declaration and must be considered by the Examiner, see MPEP 716.01.

One concern, expressed in the rejection, was that experimental data presented in the prior Declaration fail to show a synergistic effect for the combination of acetyl-L-carnitine and HCA, in part, because the scope of the claims is not commensurate in scope with the

values reported in the Declaration's Tables. To address this concern, claim 11 has been amended to recite particular amounts of acetyl-L-carnitine and HCA.

The second concern expressed in the rejection was that the results shown in the Declaration show less than an additive effect for the combination of acetyl-L-carnitine and HCA "taking into consideration the stand deviation". However, this concern is misplaced in view of the T-test results also presented in the prior Declaration. These T-test results definitively establish that the significant differences between the compared samples, and the statistical validity of the synergistic results shown in Tables 2, 4 and 5 of the prior Declaration and reproduced above. For the convenience of the Examiner, the Applicants have appended to this response an excerpt elaborating on the T-test of statistical significance from Statistics, CliffsQuickReview, Hungry Minds, Inc., New York (2001). Alternatively, if, upon review, the Examiner believes the results of record do not show the synergistic effects of the combination of acetyl-L-carnitine and HCA, the Applicants respectfully request that he make of record evidentiary support for his opinion and his exact methodology of determining statistical significance, see MPEP 2144.02 and 2144.03.

Accordingly, the Applicants respectfully request that this rejection be withdrawn in view of the amended claim language, experimental data showing the highly synergistic properties of the invention, and in view of the T-test results establishing the statistical significance of the results of record.

Rejection--35 U.S.C. 103

Claims 11-18 and 20-31 were rejected under 35 U.S.C. 103(a) as being unpatentable over Hastings, U.S. Patent 5,626,849 by itself, or in view of Wiegand, U.S. Patent 3,810,994 and/or Burtle, U.S. 5,030,657. The cited art does not render the invention obvious, because it

does not suggest that the combination of acetyl-L-carnitine and HCA would provide the synergistic properties shown in Tables 1-5. As discussed above, the prior Declaration establishes the statistically significant synergy of the combination of acetyl-L-carnitine and HCA.

Rejection--35 U.S.C. 103

Claim 18 was rejected under 35 U.S.C. 103(a) as being unpatentable over Hastings, U.S. Patent 5,626,849 by itself, or in view of Wiegand, U.S. Patent 3,810,994 or Burtle, U.S. Patent 5,030,657, or both, and further in view of page 4 of the specification. Page 4 of the specification was cited for its teaching that HCA may be obtained from certain plant sources. However, as the cited prior art references do not suggest the synergistic effects of the combination of acetyl-L-carnitine and HCA, the Applicants submit that Claim 18 is also not obvious for the reasons state above.

Rejection--35 U.S.C. 103

Claim 23 was rejected under 35 U.S.C. 103(a) as being unpatentable over Hastings, U.S. Patent 5,626,849 by itself, or in view of Wiegand, U.S. Patent 3,810,994 or Burtle, U.S. Patent 5,030,657, or both, and further in view of Weiner (1989) by itself, or in combination with Stracher, U.S. Patent 5,008,288. The Applicants submit that Claim 23 is not obvious for the reasons set forth above. Weiner is cited for teachings of liposomes as drug delivery agents and Stracher as teaching carnitine incorporation into liposomes. The compositions comprising acetyl-L-carnitine and HCA are not obvious for the reasons set forth above--there is no motivation to combine acetyl-L-carnitine and HCA or any suggestion of the superior, synergistic properties of this combination. As the basic combination of acetyl-L-carnitine

and HCA of the present invention is not obvious for the reasons set forth above, then liposomes comprising this combination would also not be obvious.

Rejection--35 U.S.C. 103

Claims 28-30 were rejected under 35 U.S.C. 103(a) as being unpatentable over Wiegand, U.S. Patent 3,810,994 or Burtle, U.S. Patent 5,030,657; or Wiegand, U.S. Patent 3,810,994, in view of Moffett, U.S. Patent 5,536,516; or Hastings, U.S. Patent 5,626,849 by itself, or in view of Wiegand and/or Burtle, and further in view of Cavazza, U.S. Patent 4,268,524.

Wiegand, Burtle, Moffett and Hastings have been addressed above. Briefly, these documents do not disclose or suggest compositions comprising acetyl-L-carnitine and HCA or suggest the superior, synergistic properties of this combination.

Cavazza is generally directed to a method of using acylcarnitines to increase levels of high-density lipoproteins. While Table 4 of Cavazza indicates the effects of acylcarnitines on serum lipids, it does not disclose or suggest the surprising, superior and synergistic properties of the combination of acetyl-L-carnitine and HCA. As shown in Tables 4 and 5 of the attached Declaration this combination provides highly significant reductions in triglycerides and cholesterol levels compared to acetyl-L-carnitine alone or HCA alone. The superior and synergistic effects of the combination of acetyl-L-carnitine and HCA are not suggested by Cavazza or the other cited art. Accordingly, the Applicants respectfully request that this ground of rejection also be withdrawn.

CONCLUSION

In view of the above amendments and remarks, the Applicants respectfully submit that Claims 11-18 and 20-31 are now in condition for allowance. Early notification to that effect is earnestly solicited.

Respectfully submitted,

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Attachment: Statistics, CliffsQuickReview (2001), pages 62-87.

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Docket No.:	<u>200427US0 CONT</u>
Serial No:	<u>09/777,874</u>
Amendment Filed:	_____

IN THE CLAIMS

Please amend claim 11 as follows:

--11. (Twice amended) A composition comprising:

(i) a first component selected from the group consisting of acetyl L-carnitine, a salt thereof and an ester thereof; and

(ii) a second component selected from the group consisting of a hydroxycitric acid and a hydroxycitric acid derivative,

wherein said composition comprises at least 2 gr of component (i) per 100 gr and 1 gr of component (ii) per 100 grams.

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